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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1646	9

DATE MAILED: 12/16/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 10-19-98.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 38-39, 49-67 is/are pending in the application.

Of the above, claim(s) 59-67 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 38-39, 49-58 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

☐ Interview Summary, PTO-413

☑ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

* U.S. GPO: 1996-410-238/40050

DETAILED ACTION

1. Applicant's election of Group I (claims 38-39, 49-58) in Paper No. 8, 10/19/98, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 59-67 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. It is suggested that the title be amended to recite " antibodies to chemokine receptor 3".

3. The disclosure is objected to because of the following informalities:

On page 17, lines 22-25, the old address of ATCC in Rockville, MD is disclosed. The new address is ATCC, 10801 University Boulevard, Manassas, VA 20110-2209.

Appropriate correction in the specification is required.

Claim rejections-35 USC § 112

4. Claim 58 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The hybridoma cell line recited in claim 58 is essential to the claimed invention. The reproduction of antibodies from the disclosed hybridomas is an extremely unpredictable event. The hybridomas 7B11, disclosed on page 17, lines 22-25, of the specification, must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The instant specification does not disclose a repeatable process to obtain the hybridomas, and it is not apparent if the hybridomas are readily available to the public. If the deposits have been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the hybridomas have been deposited under the Budapest Treaty and that the hybridomas will be irrevocably and without restriction or condition be released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample or for the enforceable life of the patent whichever is longer. See 37 CFR 1.806. If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

Amendment of the specification to disclose the date of deposit and the complete name and address of the depository is required.

If the deposit was made after the effective filing date of the application for a patent in the United States, a verified statement is required from a person in a position to corroborate that the hybridomas described in the specification as filed are the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to *In re Lundak*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985), and 37 CFR 1.801-1.809 for further information concerning deposit practice.

5. Claims 49 and 53 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 49 and 53 recite "...binding specificity for a mammalian chemokine receptor 3 protein", which is not described in the specification. The specification (page 36, lines 10-19) discloses the antibodies of the present invention have specificity for human CKR3 and have an epitopic specificity similar to that of murine 7B11 monoclonal antibody described therein. However, the specification teaches only the antibodies to human CKR3 (pages 59-77) but does not teach antibodies (other than the monoclonal antibodies disclosed), to any other mammalian receptor. The specification does not

disclose the amino acid sequences for the other mammalian CKR3 receptors i.e. bovine, ovine, porcine, equine, feline, etc. with respect to the disclosure of relevant identifying characteristics i.e. structure, other physical and/or chemical characteristics or combination of such characteristics. The description for mammalian CKR3 receptors is limited to their function, and to a method for isolating the claimed sequence from its natural source. A sequence described only by a purely functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed species. In this case, even though a genetic code table would correlate the human CKR3 amino acid sequence with a genus of coding nucleic acids, the same table cannot predict the native, naturally occurring nucleic acid sequence of feline or canine mRNA or its corresponding cDNA and protein sequence. Thus, at the time the application was filed, antibodies to mammalian CKR3 was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention.

6. Claims 38-39, 49-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody which binds a human chemokine receptor 3 (CKR3) protein having the amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO:4, does not reasonably provide enablement for "all" antibodies or functional portions thereof which bind to a mammalian chemokine receptor 3 protein or portion of said receptor protein. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

With respect to claims 38-39 and 49-58 as recited, what is claimed in the instant invention broadly encompasses "all" antibodies or functional portions thereof which bind to a mammalian chemokine receptor 3 protein or portion of said receptor protein. While the specification discloses that the antibodies of the present invention have specificity for human CKR3 (see page 36, lines 10-12) and this is the biological property which the antibodies are expected to exhibit, the specification is non-enabling for the unlimited number of antibodies and which are encompassed by the scope of the claims in the absence of structural limitations regarding human CKR3 recited in the claims. Claim 38, claim 49 and claim 53 is each a single means claim (M.P.E.P. 2164.08(a)). In In re Hyatt, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), the Courts have held that: "A single means claim, i.e. where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph." (A single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification disclosed at most only those means known to the inventor). Since no material limitations for the protein have been recited in the claims and only a biological activity has been recited, the claims encompass every conceivable structure (means) for achieving the stated property (result), a fact situation comparable to Hyatt. Therefore, not only antibodies against the instant human CKR3, but any other antibodies that can bind other receptor proteins are encompassed by the scope of the claim in the absence of material limitations regarding

the instant human CKR3 receptor recited in the claims. The claimed invention encompasses antibodies not envisioned or described in the specification, and neither does the specification disclose how these claimed antibodies can be distinguished from each other. The specification only enables antibodies to the human CKR3 protein having the amino acid sequences shown in SEQ ID NO:2 and SEQ ID NO:4, the polypeptides having specific characteristics and properties. These properties may differ structurally, chemically and physically from other known proteins. By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) quantity of experimentation, (2) guidance presented, (3) the predictability of the art, and (4) the breadth of the claims, in the instant application, the quantity of experimentation to determine which other antibodies binding to proteins, are encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little, thereby rendering the results of the assays taught in the specification unpredictable (see pages 128-130, Example 13). Therefore, it would require undue experimentation to determine which antibodies would be encompassed by the scope of the claims. The disclosure of a single antibody is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims which encompass every and all antibodies to CKR3 receptor polypeptides, including mutants of the polypeptides. In In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), the Courts have held that:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work;

however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Furthermore, the amount of embodiments corresponding to the desirable antibodies, may be innumerable, and the enabled embodiments amount to only one. Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe any other polypeptides other than those whose amino acid sequences are shown in SEQ ID NO:2 and SEQ ID NO:4, and since it is deemed to constitute undue experimentation to determine antibodies to all the others, the disclosure is not commensurate with the scope of the claims. Therefore, Applicants are not enabled for antibodies to a protein having anything less than the amino acid sequences shown in SEQ ID NOS:2 and 4. It is suggested that by employing conventional claim language, the preamble to claim 38 read approximately as follows: "an antibody to a human chemokine receptor 3 protein said protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4....".

Claims 38 and 49, 50, 53, each recite "portion of said receptor protein", which limitations are non-enabled by the specification in the absence of reference to a subset of amino acid sequences comprising the domains to which the functional properties of the receptor polypeptide have been

ascribed. While the specification discloses that the antibodies of the present invention have specificity for human CKR-3 (CCR-3) protein (see page 36, lines 10-12), it provides no guidance as to which amino acids might comprise the minimum residues of a fragment which retains any enabled functional property peculiar to the instant receptor polypeptides. One would not have a reasonable expectation of successfully making a representative number of amino acid fragments which bind the claimed antibody, consistent with the scope of the claims. Additionally, one would reasonably expect that fragmentation of the 355 amino acid residue polypeptides would abolish activity because activity is determined not only by primary sequence, but also by three-dimensional structure, as, for example, is the case for the ligand binding site of a receptor or for a catalytic site of an enzyme. Any arbitrary fragment of the amino acid sequence of SEQ ID NO:2 or 4 would not be expected to confer the production of antibodies such that these antibodies would block binding of ligand to the CCKR3 receptor. Only specific antibodies to the extra-cellular region of the receptor, the region being involved in ligand binding, would be expected to block ligand binding to the CKR3 receptor. Therefore, in the absence of delimiting amino acid sequences that make up the functional domains of the instant receptor proteins, a person of ordinary skill in the art would be unable to make antibodies to fragments of the amino acid sequences of the receptor, as embraced by the claims without undue experimentation to determine which fragments have biological activity i.e. are involved in ligand binding to the CCKR3 receptor.

7. Claims 38-39 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38, line 1 is rejected as vague and indefinite because it is unclear from the recitation of "functional portion thereof" which function Applicants intend to claim. It is suggested that Applicants amend the claim to recite the specific function supported by the instant specification.

Claim 39 is rejected as vague and indefinite insofar as it depends on claim 38 for this limitation.

Claim rejections-35 U.S.C. 101 provisional double patenting rejection

8. Claims 49-52 are provisionally rejected under 35 U.S.C. 101 as being substantial duplicates of claims 53-56, respectively. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to reject the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9a. Claims 38-39 and 49-50, are rejected under 35 U.S.C. § 103 as being unpatentable over Yamagami et al. (1994) in view of Lerner (1982) and Harlow et al. (1988).

Yamagami et al. discloses the cDNA cloning, the predicted amino acid sequence and functional expression of a human monocyte chemoattractant protein 1 receptor (page 1156, see abstract; page 1159, Figure 1; page 1161, Figure 3), the reference receptor having a stretch of 10 amino acids identical (residues 140-148) with the amino acid sequence depicted in SEQ ID NO:2 of the instant application, these 10 residues not being part of the transmembrane domain. A copy of the comparison of SEQ ID NO:2 (SEQUENCE COMPARISON 'A') in the instant invention and the amino acid sequences of the protein in the reference is enclosed at the end of this office action. Yamagami et al. fail to disclose antibodies to the human monocyte chemoattractant protein 1 receptor encoded by the cDNA.

Lerner teaches the production of antibodies from known polypeptides, wherein the antibody can have predetermined specificity and in addition can be of a single specificity (i.e. a monoclonal) (see abstract, page 592; and first paragraph). Lerner also teaches that antibodies made against a predetermined peptide, are useful in studying the protein conformation of the intact protein from which the immunizing peptide was cleaved from (column 2, page 594, last 8 lines on page). Further, Harlow et al. teach that peptides of six residues in length will consistently elicit antibodies that bind to the original protein (page 76, third paragraph, especially lines 21-22)

Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to use the amino acid sequences taught by Yamagami et al., to produce monoclonal and polyclonal antibodies with a predetermined specificity as taught by Lerner with the expectation that these antibodies made against proteins with sequence identity to SEQ ID NO:2 would be useful in understanding the conformational changes the receptor undergoes during activation by a natural ligand.

Conclusion

No claim is allowed

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (703) 308-4229. The examiner can normally be reached on Monday-Friday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached on (703) 308-2731.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Prema Mertz

Prema Mertz Ph.D.
Patent Examiner
Art Unit 1646
December 11, 1998